DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

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James J. Schumann, Esq.
FITCH, EVEN, TABIN & FLANNERY for
THE SALK INSTITUTE FOR BIOLOGICAL STUDIES
4250 Executive Square, Suite 510
La Jolla, CA 92037

Re: Docket No. 92E-0133

Dear Mr. Schumann:

This is in response to your request for redetermination of the beginning of the testing phase for Supprelin, as stated in the June 2, 1992 Federal Register Notice (57 Fed. Reg. 23,237), submitted on behalf of The Salk Institute for Biological Studies. The request for redetermination asks FDA to use a later IND for purposes of determining of the beginning of the testing phase of Supprelin for patent term restoration. *We are denying your request for redetermination for the reasons stated in this letter.*

The request for redetermination argued that the testing phase for Supprelin began on the day an existing IND was modified to permit use of the active ingredient in Supprelin, histrelin acetate ("histrelin"), for the indicated use of precocious puberty. The request for redetermination pointed out that the later studies using histrelin for precocious puberty constituted the pertinent investigational work with respect to the use of histrelin for precocious puberty. The request for redetermination, however, acknowledged that the later study using histrelin for precocious puberty was related to an earlier IND to use histrelin for endometriosis. In addition, the request for redetermination acknowledged that the clinical investigators involved in the histrelin study for precocious puberty were authorized to cross reference the earlier IND for purposes of chemistry, toxicology and similar information.

In general in the case of multiple INDs, FDA has used the first IND of the active ingredient of the drug product as the beginning of the testing phase, because information derived from this first IND was or could have been relied on or was relevant for approval to market the drug product. This is in accord with the explanation provided in the preamble to the final regulation which states:

> For drugs for which more than one exemption is in effect, the provisions of the patent extension statute specifically state that the testing phase for human drug products begins on the date an exemption 'under subsection (i) of section 505 or subsection (d) of section 507 became effective for the approved human drug product' (35 U.S.C. 156(g)(B)(i)). Thus, while the drug's dosage form and strength during the IND phase need not be identical to that of the approved drug product, the information

> from the IND studies must have been material to the approval of the drug product. Where multiple INDs are in effect, the agency will consider the testing phase to have begun when the first IND for the approved human drug product became effective.

While the preamble utilized the example of different dosage forms and strengths, the explanation applies to INDs involving different indications as well.

In the case of Supprelin, the request for redetermination indicates that at least some information could have been relied on from the earlier IND. In fact, the request specifically mentioned that information regarding chemistry and toxicology could be relied on, which FDA considers material to the approval of a drug product. Therefore, the appropriate beginning of the testing phase for Supprelin is the date of the first IND for its active ingredient, histrelin acetate.

For these reasons, your request for redetermination of the beginning of the testing phase for Supprelin is denied.

Sincerely yours,

Stuart L. Nightingale

Stuart L. Nightingale, M.D.
Associate Commissioner for
Health Affairs